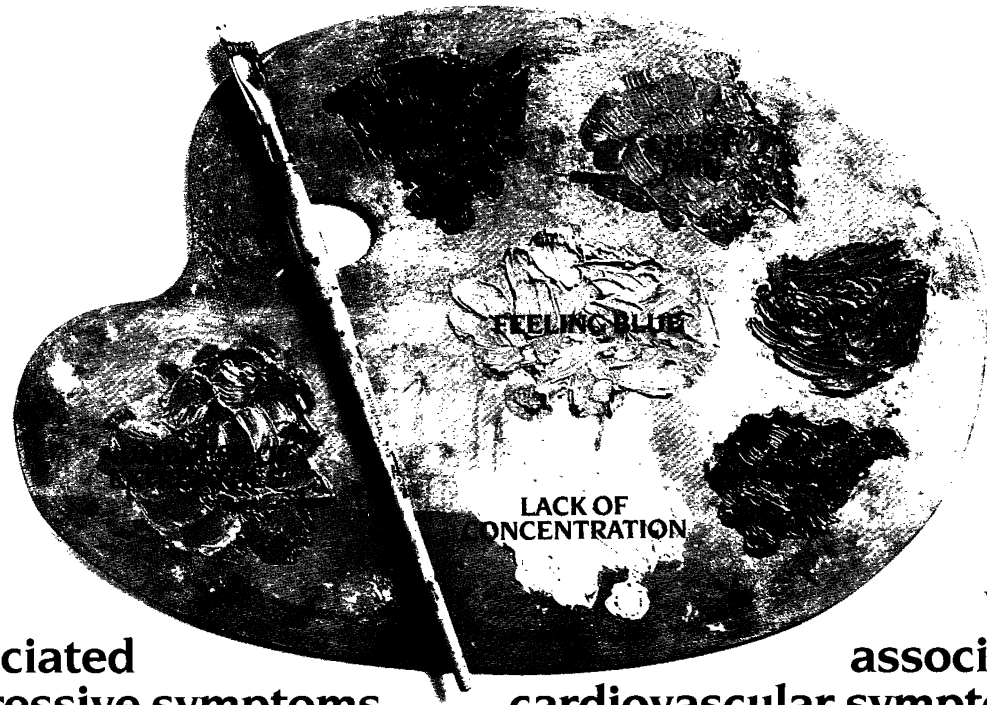
The portrait of anxiety

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001 USA

Please see adjacent page for brief summary of prescribing information.

is often complicated

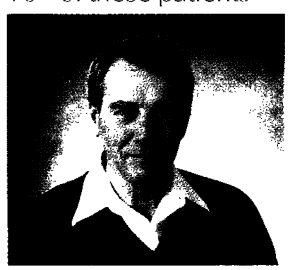


With associated depressive symptoms.

In double-blind four-week clinical trials in 632 patients with moderate to severe anxiety, therapy with XANAX was compared with placebo.

XANAX was significantly more effective ($P<.001$) than placebo in relieving the anxiety, with over half of the patients showing marked to moderate improvement by the first evaluation period (one week).

In addition, over 70% of these patients experienced associated moderate to severe depressed mood. XANAX was shown to be significantly more effective ($P<.014$) than placebo in improving the associated depressed mood.



With associated cardiovascular symptoms.

Almost 60% of patients in the study had anxiety with associated cardiovascular symptoms even though cardiovascular disease had been ruled out. XANAX was shown to effectively relieve anxiety including the associated cardiovascular symptoms.

XANAX, the first of a unique class—the triazolobenzodiazepines.

- *Well tolerated*—Side effects, if they occur, are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions.
- *Sustained efficacy*—No reported increase in dosage during 16-week clinical study, once an appropriate dosage was achieved. Since long-term effectiveness of XANAX has not been established, it is recommended that it not be used for longer than 16 weeks.
- *Simple dosage*—0.25 to 0.5 mg t.i.d.

TABLETS 0.25, 0.5 & 1 MG

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alprazolam IV

for the relief of complicated anxiety

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***CAPOTEN® (captopril tablets) may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. Overall, the most frequently occurring adverse reactions associated with CAPOTEN are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.**

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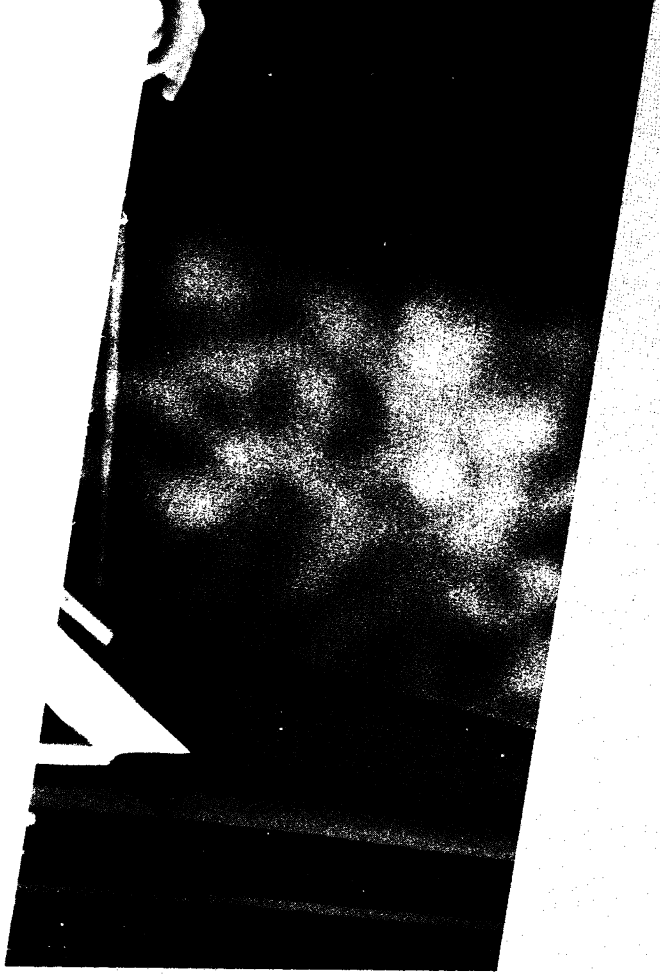
1. Croog SH, Levine S, Testa MA, et al: The effects of antihypertensive therapy on the quality of life. N Engl J Med 314(26):1657-1664, 1986.
2. Data on file, University of Connecticut.



THE CAPOTEN® (captopril tablets) DIFFERENCE

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension—CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Neutropenia/Agranulocytosis—Neutropenia ($<1000/mm^3$) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine <1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count $<1000/mm^3$) withdraw captopril and closely follow the patient's course.

Proteinuria—Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension—Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function,* Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis*—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction.

Surgery/Anesthesia—If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension: Patients on Diuretic Therapy*—Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity—In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release—Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis—Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C—There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal—About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic—Neutropenia/agranulocytosis have occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic—Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients—reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular—Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia—About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertensive patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg and 50 mg also available in bottles of 1000), and in UNIMATIC® unit-dose packs of 100 tablets. (J3-658H)

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diltiazem HCl/Marion

90mg NEW 120mg GREATER DOSAGE FLEXIBILITY

A remarkable safety profile[1-6]
The low incidence of side effects with Cardizem allows patients to feel better.

Protection against angina attacks[1,5,7-9]
The predictable efficacy of Cardizem in stable exertional and vasospastic angina allows patients to do more.*

A decrease in myocardial oxygen demand
Resulting from a lowered heart rate-blood pressure product.[5]

Compatible with other antianginals[6]†

Safe in angina with coexisting hypertension, COPD, asthma, or PVD[1,3,5,6]

**CARDIZEM® (diltiazem HCl) is indicated in the treatment of angina pectoris due to coronary artery spasm and in the management of chronic stable angina (classic effort-associated angina) in patients who cannot tolerate therapy with beta-blockers and/or nitrates or who remain symptomatic despite adequate doses of these agents.*

†See Warnings and Precautions.

Please see brief summary of prescribing information on the next page.

CARDIZEM® ANTIANGINAL PROTECTION PLUS SAFETY

diltiazem HCl/Marion

Rx Cardizem® (diltiazem HCl)
☐ 60 mg ☐ 90 mg
☐ 120 mg
Sig: tid

Usual maintenance dosage range: 180-360 mg/day

Brief Summary
Professional Use Information

CARDIZEM®
(diltiazem HCl) 30 mg, 60 mg, 90 mg, and 120 mg Tablets

CONTRAINDICATIONS
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS
1. ***Cardiac Conduction.*** *CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.*
2. ***Congestive Heart Failure.*** *Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt).*
   Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. ***Hypotension.*** *Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.*
4. ***Acute Hepatic Injury.*** *In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but probable in some. (See PRECAUTIONS.)*

PRECAUTIONS
General. *CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.*

Drug Interaction. *Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)*

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. *A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.*

Pregnancy. *Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.*

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. *Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.*

Pediatric Use. *Safety and effectiveness in children have not been established.*

ADVERSE REACTIONS
Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%):

Cardiovascular:	*Angina, arrhythmia, AV block (first degree), AV block (second or third degree — see conduction warning), bradycardia, congestive heart failure, flushing, hypotension, palpitations, syncope.*
Nervous System:	*Amnesia, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.*
Gastrointestinal:	*Anorexia, constipation, diarrhea, dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic warnings), vomiting, weight increase.*
Dermatologic:	*Petechiae, pruritus, photosensitivity, urticaria.*
Other:	*Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.*

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

Issued 9/86

See complete Professional Use Information before prescribing.

References: ***1.*** *Schroeder JS: Mod Med 1982;50(Sept):94-116.* ***2.*** *Cohn PF, Braunwald E: Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39.* ***3.*** *O'Rourke RA: Am J Cardiol 1985;56:34H-40H.* ***4.*** *McCall D, Walsh RA, Frohlich ED, et al: Curr Probl Cardiol 1985;10(8):6-80.* ***5.*** *Frishman WH, Charlap S, Goldberger J, et al: Am J Cardiol 1985;56:41H-46H.* ***6.*** *Shapiro W: Consultant 1984;24(Dec):150-159.* ***7.*** *O'Hara MJ, Khurmi NS, Bowles MJ, et al: Am J Cardiol 1984;54:477-481.* ***8.*** *Strauss WE, McIntyre KM, Parisi AF, et al: Am J Cardiol 1982; 49:560-566.* ***9.*** *Feldman RL, Pepine CJ, Whittle J, et al: Am J Cardiol 1982;49:554-559.*

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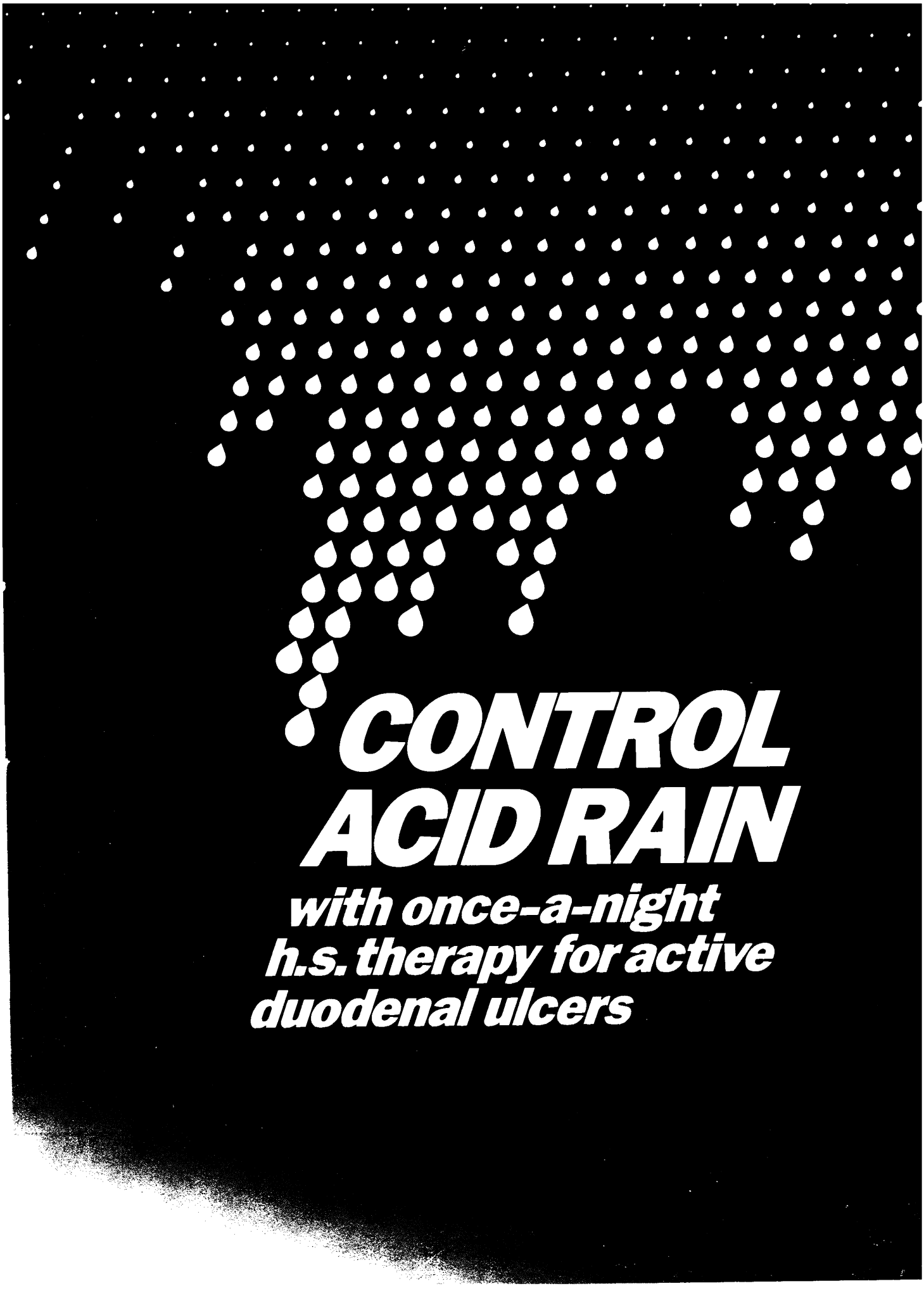
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ACID RAIN
with once-a-night
h.s. therapy for active
duodenal ulcers

Only one tablet at bedtime

Controls nocturnal acid to relieve pain and heal duodenal ulcers

Heals active duodenal ulcers after 4 weeks in most patients*[*1]

In well-controlled, double-blind, multicenter trials, ZANTAC 300 mg h.s. healed active duodenal ulcers in 84% of patients after 4 weeks. After 8 weeks, healing rates may be higher with ZANTAC 150 mg b.i.d. (92%) than with ZANTAC 300 mg h.s. (87%).

Relieves pain and other symptoms as effectively as ZANTAC 150 mg b.i.d.[1]

Zantac 300

ranitidine HCl/Glaxo 300 mg tablets

Once-daily dosing may enhance compliance in patients for whom dosing convenience is important

Side-effects profile comparable to ZANTAC 150 mg b.i.d.[1-3]

Headache – sometimes severe – has been reported. Rare effects on the CNS, cardiovascular, GI, hepatic, and integumental systems have been observed, as well as rare cases of hypersensitivity reactions. See ADVERSE REACTIONS section of Brief Summary of Product Information before prescribing.

No significant interference with the hepatic cytochrome P-450 enzyme system at recommended doses

ZANTAC 300 mg h.s. had no significant drug interactions with theophylline or warfarin. The bioavailability of certain medications whose absorption is dependent on a low gastric pH may be altered when ZANTAC or other medications which decrease gastric acidity are administered.

It is not known exactly how much acid inhibition is needed to heal ulcers.

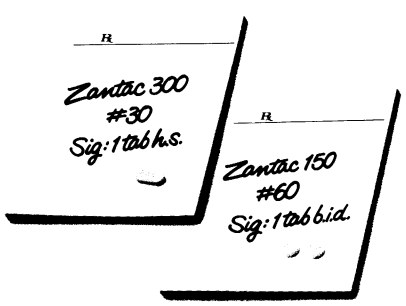
Glaxo / ROCHE

See next page for references and Brief Summary of Product Information.

IN ACTIVE DUODENAL ULCERS

Once-a-night h.s. therapy controls acid rain

Zantac® 300
ranitidine HCl/Glaxo 300 mg tablets



Two effective regimens to treat active duodenal ulcers:

References: 1. Data available on request, Glaxo Inc. **2.** Ireland A, Colin-Jones DG, Gear P, et al: Ranitidine 150 mg twice daily vs 300 mg nightly in treatment of duodenal ulcers. *Lancet* 1984;2:274-275. **3.** Colin-Jones DG, Ireland A, Gear P, et al: Reducing overnight secretion of acid to heal duodenal ulcers. *Am J Med* 1984;77 (suppl 5B):116-122.

ZANTAC® 150 Tablets **BRIEF SUMMARY**
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.
2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella, E coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: *Teratogenic Effects: Pregnancy Category B:* Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC® (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

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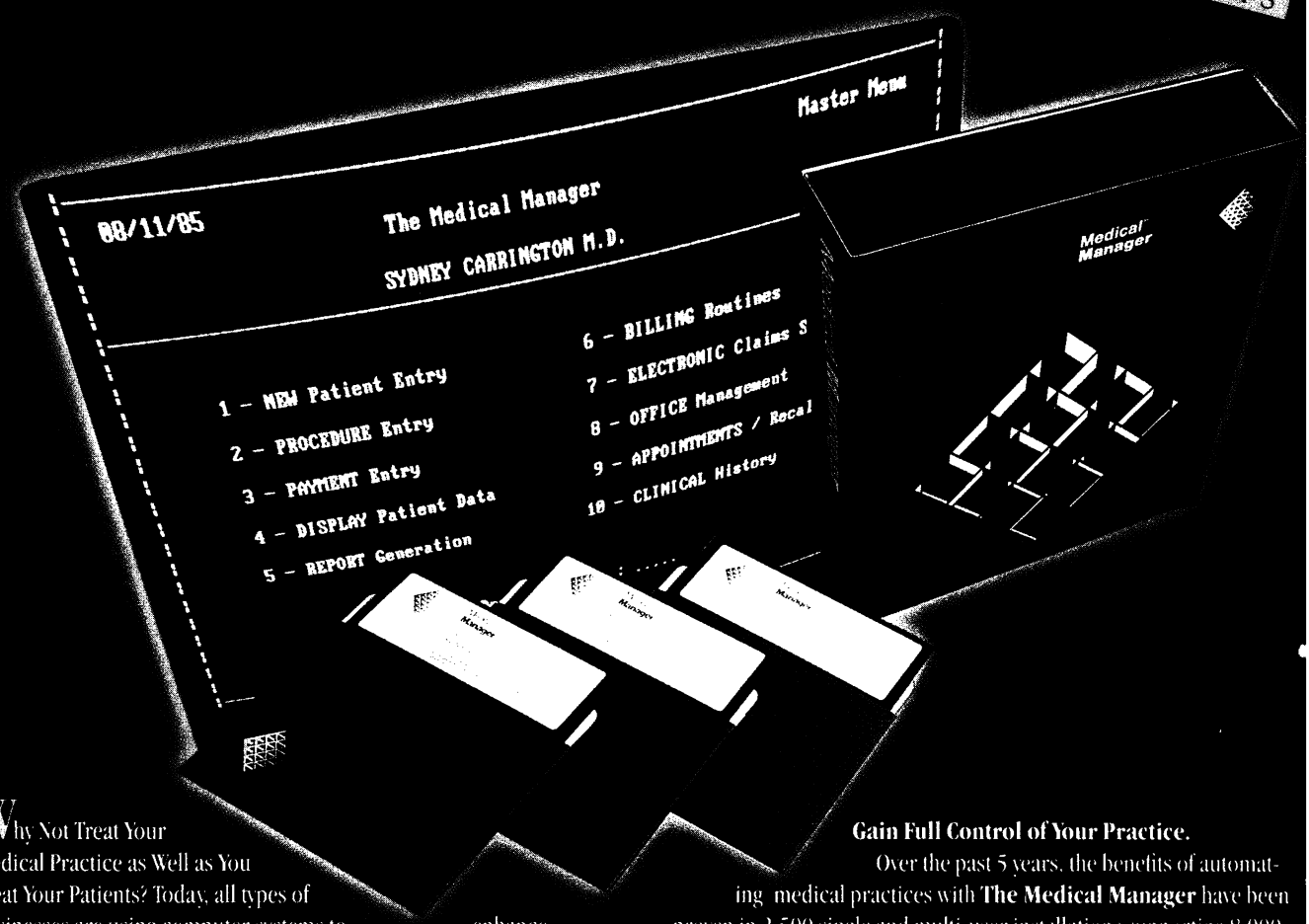

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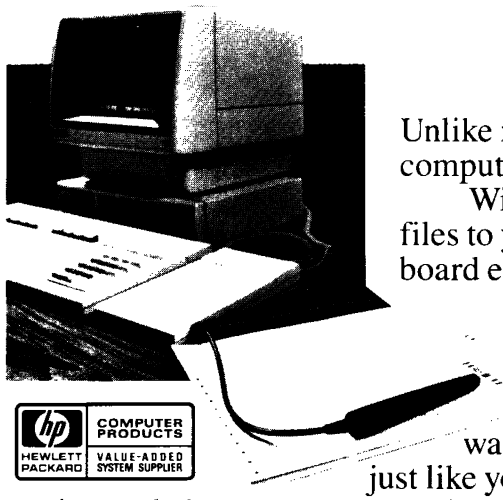

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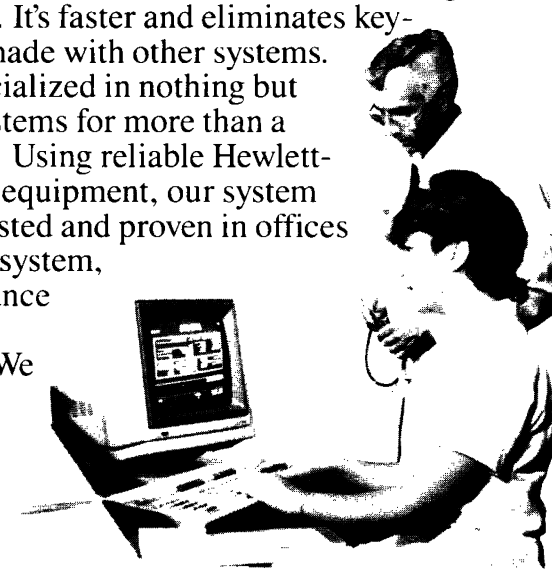

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Before prescribing, see complete prescribing information in SK&F CO. literature or PDR. The following is a brief summary.

* ***WARNING***

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: *Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.*

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. *If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake.* ***Associated widened QRS complex or arrhythmia requires prompt additional therapy.*** *Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.*

Precautions: *The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin-converting enzyme (ACE) inhibitors can elevate serum potassium; use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function. Thiazides may add to or potentiate the action of other antihypertensive drugs. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.*

Adverse Reactions: *Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.*

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); In Patient-Pak™ unit-of-use bottles of 100.

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(Continued on Page 764)

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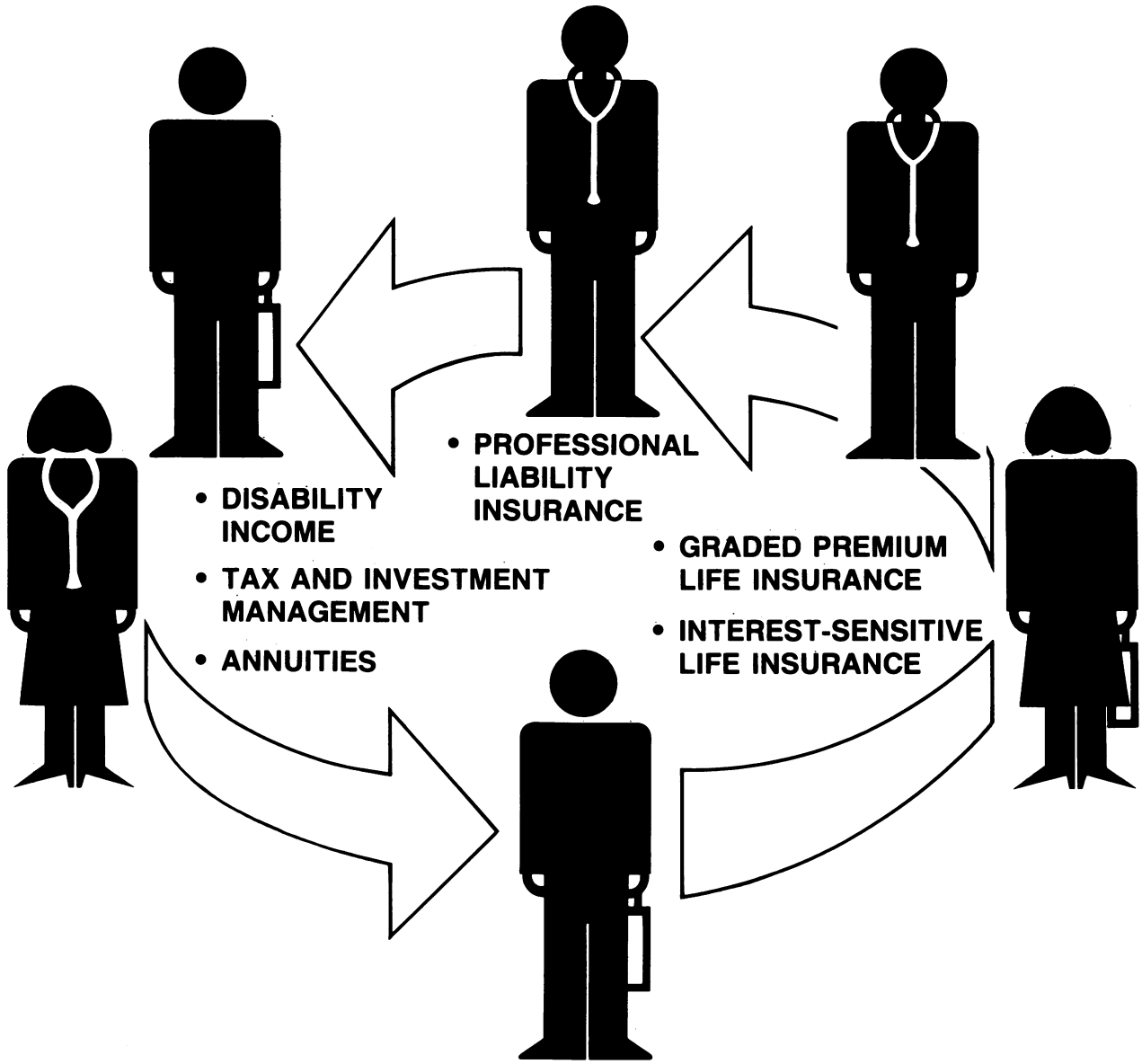


Choose the professionals. Through our subsidiary, The Doctors' Company Insurance Services, we offer physicians the convenience of a comprehensive source for income protection and financial planning services.

THE DOCTORS' COMPANY

401 WILSHIRE BOULEVARD, SANTA MONICA, CA 90401
(213) 451-3011 (800) 352-7271 (CALIFORNIA) (800) 421-2368 (OUTSIDE CALIFORNIA)

(Continued from Page 764)

PHYSICIANS WANTED

OCCUPATIONAL/FAMILY PRACTICE. Excellent opportunities with the west coast's leading provider of Occupational/Family Practice medicine. Full-time/part-time positions throughout California and Washington (Seattle/Tacoma). Current license/CPR. Prior outpatient/family practice/industrial-type trauma experience. Attractive salary/incentives/benefits/malpractice. Contact Personnel Director, ReadiCare, Inc., 446 Oakmead Parkway, Sunnyvale, CA 94086; (800) 237-3234. Join our dynamic team of professionals. Practice and live in an incomparable environment.

PARTNER DESIRED—BC/BE Radiologist to share hospital and office practice. Must enjoy general radiology, mammography, nuclear medicine, ultrasound and CT. Hands on experience in real time ultrasound helpful. Excellent salary and benefits. Early partnership. Will consider longer term locums. Send CV to Radiology, 5681 N. Fresno St, Fresno, CA 93710.

SAN FRANCISCO BAY AREA multispecialty group seeks Family Practitioner, BC/BE, to join 26 congenial men and women delivering quality care in a combined fee-for-service, HMO/PPO setting. Bay Valley Medical Group, Attn: Don Lass, 27212 Calaroga Ave, Hayward, CA 94545; (415) 785-5000.

ORTHOPEDIST. The west coast's leading Occupational/Family Practice medical provider has full-time/part-time opportunities for Orthopedic Specialist in California and Washington (Seattle/Tacoma). Attractive package includes: guaranteed salary, incentive bonus and benefits. Current license. Contact Personnel Director, ReadiCare, Inc., 446 Oakmead Parkway, Sunnyvale, CA 94086; (800) 237-3234. Join our dynamic team of professionals. Practice and live in an incomparable environment.

OREGON—FAMILY PRACTITIONERS, INTERNISTS, PEDIATRICIANS. Private practice opportunities are immediately available in beautiful northwest Oregon. Call today to investigate this opportunity to practice challenging medicine in a hospital-supported surrounding, while enjoying an incomparable lifestyle in one of the Northwest's most scenic areas. Competitive first year guarantees offered to the selected candidate. Interview and relocation expenses absorbed by the client. For complete details, contact Jim Murphy, Spectrum Search, PO Box 27352, St. Louis, MO 63141; 1 (800) 237-6906; (314) 878-2280.

CHAIRMAN, DEPARTMENT OF INTERNAL MEDICINE, KERN MEDICAL CENTER. A county operated teaching hospital is seeking a chairman for this UCLA affiliated department. The department has nine full-time and part-time members, 18 residency positions all currently filled with quality graduates. Qualifications: BC in Internal Medicine, established record of scholarly achievement in teaching and patient care, demonstrated management skills to direct a fully accredited residency program in an active public hospital and relate to other programs at Kern Medical Center and the UCLA system. Candidate must be eligible for appointment to senior faculty position at UCLA and be licensed in the State of California. (The County of Kern is an Equal Opportunity Employer.) Address inquiries with CV to Paul Toot, MD, Chairman, Internal Medicine Search Committee, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

NEW MEXICO—FAMILY PHYSICIAN. Innovative practice in New Mexico mountain community needs third BC/BE FP. Salary guarantee with reasonable work schedule. Video available showing our practice style, area, and people. Gila Family Care, 1121 West St, Silver City, NM 88061.

INTERNIST, BC, to join four others in a busy practice in pleasant Sierra foothills community. Abundant recreational opportunities, yet near urban centers. Contact Dennis Nousaine, MD, FACP, 815 Court St, Ste 7, Jackson, CA 95642.

PHYSICIANS WANTED

PHYSICIANS WANTED

PART-TIME MEDICAL CONSULTANT CONTRACTS

Physicians needed to work under contract, on a part-time basis for the Social Security Administration's Disability Insurance Program, involves review of medical evidence in disability claims at 100 Van Ness Ave, San Francisco, California. No patient contact. Applicants must: (1) have a valid license to practice medicine in the US; (2) have current or recent clinical experience; and (3) be available between 7:00 am and 5:30 pm, Monday through Friday for case review. Subject to change, the specialties needed are Orthopedics, Physiatry and Internal Medicine. Women and minorities are encouraged to apply. If interested in applying, please submit a letter of interest or call Perlena Turner at (415) 556-8852 by December 23, 1987 (collect calls are not accepted).

MAIL TO: Contracting Officer
Department of Health and Human Services
50 United Nations Plaza, Room 403
San Francisco, CA 94102

THE COMMUNITY OF ARTESIA, NEW MEXICO is seeking a BC/BE General Surgeon to establish a private practice. Fully-equipped office with established referral patterns available for purchase. Community-based financial assistance may be available to the right individual. Artesia is a community of 14,000 located in southeast New Mexico. A great place to raise a family—peaceful community with year 'round recreation and excellent weather. Fully-equipped, 38-bed new hospital. Please submit CV to Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666; or, call 1 (800) 545-4030, ext. 8300.

FAMILY PRACTITIONER. Tulare County is seeking a BE/BC Family Practitioner to practice in an out-patient clinic which includes inpatient duties, with 14 physicians. Ability to perform simple OB required. The County provides a benefit package which includes malpractice insurance coverage. Consider a semi-rural lifestyle with cultural amenities of metropolitan areas easily accessed and Kings Canyon and Sequoia National Park nearby. Salary $89,724-$94,296 annually. Send CV to Tulare County Personnel, 2900 W. Burrel, Visalia, CA 93291, (209) 733-6266; Equal Opportunity Employer.

FAMILY PRACTITIONER. Visalia Medical Clinic has an opening for a BC/BE Family Practitioner to join a four-physician department. Located in the San Joaquin Valley of California, serving a market area of approximately 350,000 citizens, the Visalia Medical Clinic is a 40 physician multispecialty clinic. Excellent hospital services and facilities. Compensation is incentive oriented with advancement to full partnership after one year. Excellent fringe benefits. John G. Heinsohn, Administrator, 5400 W. Hillsdale, Visalia, CA 93291; (209) 733-5222.

EUGENE, OREGON. Well-established, eight physician Family Practice group is seeking BC/BE Family Physician with interest in OB. Anticipate partnership after one year. Exceptional cultural and recreational opportunities. Home of University of Oregon. Please send CV to Rob Daugherty, MD, or Kendall Hills, MD, River Road Medical Group, 2400 River Rd, Eugene OR 97404, or call (503) 688-7527.

INTERNISTS. MED Group operates a growing suburban Sacramento area network of successful ambulatory care centers. We seek several talented, personable BE/BC Internists to develop and maintain traditional IM practices at each of our centers from the many patient referrals we generate. Compensation package includes a salary guarantee ($80,000), revenue sharing, malpractice insurance, vacation, CME stipends and other benefits. Contact Daniel Newman, MD, MED Group, 3441 Arden Way, Sacramento, CA 95825; (916) 487-7777.

UTAH. Full-time physicians needed for urgent care centers in Ogden area. Send CV to Val Rollins, MD, Emergency Department, St. Benedicts Hospital, 5475 S. 500 East, Ogden, UT 84405; or call (801) 479-2376.

URGENT CARE/INTERNAL MEDICINE/ENDOCRINOLOGY/PEDIATRICS physicians, BC/BE needed immediately to join expanding multispecialty group. Practice in rapidly growing southwest community (population 500,000 plus). Fee-for-service and prepaid health care. Group includes Family Practice/Pediatrics/Internal Medicine/Subspecialties/24-hour Urgent Care. Position offers excellent compensation and benefits plus full pension and profit sharing. Relocation expenses. Interested individuals should reply with CV to Southwest Medical Associates, PO Box 15645, Las Vegas, NV 89114-5645.

THE PERFECT PARTNERSHIP. We handle the business. You practice medicine. And we both prosper. MED Group is a growing Sacramento and Ventura County area network of sophisticated convenient emergency and family medical care centers. We have full-time and part-time openings for talented, personable physicians who can build practices by providing top-quality medical care. BC in IM, FP or EM is preferred. Some of the outstanding MED Group benefits include directorship opportunities, flexible scheduling with no overnight call, an updated compensation plan featuring attractive salaries ($75,000-$105,000 annually for 45-hour weeks), guaranteed profit sharing, equity participation through annual stock option grants, health insurance coverage, two weeks paid vacation, paid malpractice insurance, CME stipends, franchise-model practice ownership plans and more. For additional information, please call or send your CV in confidence to Charles Pietrafesa, MD, MED Group, 12327 Santa Monica Blvd, Los Angeles, CA 90025; (213) 826-1805.

RESEARCH ASSOCIATE—GASTROENTEROLOGY. Research industrial work health hazards including asbestos research. Collect and analyze data on workers exposed to hazardous materials. Evaluate cases, advise, and consult with administration and physicians regarding treatment. Research development of diagnostic and treatment procedures. Requires doctorate in Gastroenterology and four years experience same or four years Gastroenterological research experience. $3,920 per month. Job site and interview: Long Beach, California. Send resume to Job #MA11523, PO Box 9560, Sacramento, CA 95823-0560 no later than January 11, 1988.

MARIN COUNTY, CALIFORNIA, ORTHOPEDIC SURGEON to join established growing, multispecialty group. BC/BE required. This group of 55 plus physicians provides care to both fee-for-service and prepaid patients. Excellent practice opportunity and superb living conditions. Guaranteed starting salary with ownership potential. Send CV to RVMC, Inc., 1350 S. Eliseo Dr, Greenbrae, CA 94904, Attn: Personnel.

INTERNIST NEEDED FULL-TIME. Primary Care position for Board certified Internist is now available with a growing San Francisco Health Plan. The position includes both inpatient and outpatient responsibilities. Send CV to Medical Director, French Health Plan, 4131 Geary Blvd, San Francisco, CA 94118.

(Continued on Page 767)

Nevada Academy of Family Physicians 20th Anniversary

WINTER ASSEMBLY

January 31–February 5, 1988
Caesars Tahoe Hotel—Stateline, Nevada
Chairman: Richard C. Inskip, MD, AAFP Past President

The "original and still the best" CME/SKI meeting in the West!

- Outstanding scientific program, with special guest speaker, astronaut Wally Schirra
- 34 CME credits, AAFP/AMA
- United Air Lines travel discount
- Daily skiing at Heavenly Valley and other nearby resorts
- Nastar-sanctioned races; trophies and prizes
- Hosted social functions nightly
- Racquetball tournament; trophies awarded
- Spouse program
- Deluxe hotel accommodations ($74 single, $79 double)
  (Indoor pool, health club/spa, entertainment and gaming, covered parking, child care)

Registration fee: $400 Practicing Physicians
$300 Residents, Retirees, Nurses, PAs

Includes all scientific sessions, breakfasts, coffee breaks, spouse program, plus admission for 2 adults to all evening social events and awards banquet.

For more information call or write:

NEVADA ACADEMY OF FAMILY PHYSICIANS
P.O. Box 7471 • Reno, NV 89510 • 702/826-5100

(Continued from Page 766)

PHYSICIANS WANTED

INTERNAL MEDICINE—CENTRAL UTAH. Seeking General Internist and/or Internist with subspecialty in Endocrinology or Infectious Disease to join established Internal Medicine clinic. 350-bed hospital across the street. First year salary with possible partnership after first year. Inquire: Dorothy Farnworth, Central Utah Medical Clinic, 1055 North 500 West, Provo, UT 84601.

EMERGENCY MEDICINE. We are an established 35 physician partnership in northern California and we are seeking BE/BC Emergency Physicians to join us. All of our facilities have moderate volumes, many serve as EMS base stations. Salary and benefits are competitive; malpractice is paid. If interested in a career in Emergency Medicine with us, please contact Sacramento Emergency Medical Group, 4325 Auburn Blvd, Ste 100, Sacramento, CA 95841.

PHYSICIANS WANTED

THE IRVINE MEDICAL CENTER AND THE UNIVERSITY OF CALIFORNIA-IRVINE, DEPARTMENT OF RADIOLOGICAL SCIENCES are seeking a full-time faculty member for the Department of Radiological Sciences at the Clinical Associate Professor or Clinical Professor level who would be assigned as Director of the Department of Radiology at Irvine Medical Center. The Irvine Medical Center is a new 177-bed hospital currently under construction in Irvine, California. Hospital opening is scheduled for fall of 1988. Administrative experience and academic background, including teaching and/or research, is required. Please send CV and the names of five references to Richard M. Friedenberg, MD, Professor and Chairman, Department of Radiological Sciences, University of California, Irvine, 101 City Drive South, Orange, CA 92668. The University of California is an Affirmative Action and an Equal Opportunity Employer.

PHYSICIANS WANTED

SOUTHERN CALIFORNIA COASTAL COMMUNITY, FP/IM physicians with acute care skills needed to join primary care/ambulatory care practice. State-of-the-art hospital affiliated facilities located in highly desirable areas. Fee-for-service with administrative opportunities and early partnership status. Contact J. Lewis, MD, Executive Director, (714) 891-9008 or (213) 618-9200.

INTERNAL MEDICINE. Full-time position for a BC/BE Internist in a 15 resident, seven faculty, rural Family Medicine program affiliated with the University of California, Davis. Duties will include supervising residents on the medical ward and in the ICU/CCU areas. Excellent salary. Send inquiries with CV to E. Hughell, MD, Director, Family Practice Residency Program, Merced Community Medical Center, PO Box 231, Merced, CA 95340; (209) 385-7172. EOE

(Continued on Page 768)

(Continued from Page 767)

PHYSICIANS WANTED

WASHINGTON STATE
Growing
Puget Sound Community

Leading multispecialty group of 14 to add:

- ENT
- PSYCHIATRIST
- GENERAL SURGEON
- ORTHOPEDIST
- NEUROLOGIST
- OB/GYN

Private practice option. Share expenses with well-structured group. Twenty minutes to 230-bed hospital. Female and male applicants encouraged. Young population, waterfront setting. One hour to Seattle.

The Friedrich Group, Inc.
9284 Ferncliff Northeast
Bainbridge Island, WA 98110
(206) 547-7850 or (206) 842-5248

OB/GYN, CALIFORNIA, CENTRAL SAN JOAQUIN VALLEY. County sponsored, sixteen (16) physician multispecialty group practice with three (3) satellite locations is looking for a BC/BE OB/GYN to provide ambulatory, delivery, and surgical services. Committed to high quality care. The position provides a comprehensive benefit package and includes malpractice insurance coverage. Consider a semirural life-style with cultural amenities and easy access to metropolitan areas, the Sierra Nevada Mountains, and the Pacific Ocean. Salary $98,112-$103,116 annually. Send CV to Michael L. MacLean, MD, Hillman Health Center, 1062 South "K" St, Tulare, CA 93274; (209) 688-2015. Equal Opportunity Employer.

CALIFORNIA, SAN FRANCISCO BAY AREA. Full-time career Emergency Physician wanted for high volume Emergency department. Emergency Medicine BC/BE mandatory to participate in a group of twenty full-time staff physicians seeing over 300 patients per day. Salaried position, excellent benefits include three weeks paid vacation, one week CME, paid malpractice, health and life insurance, corporate shareholdership in three years. Send CV or contact David Gallagher, MD, 27400 Hesperian Blvd, Hayward, CA 94545.

CHIEF RESIDENT AND RII OR III POSITIONS. The University of Nevada School of Medicine is seeking a Chief Resident and several RII or RIII positions with the Department of Internal Medicine. Must be eligible for licensure in Nevada. Salary dependent upon qualifications. Send letter of application and two reference letters to Roger K. Ferguson, MD, Chairman, Department of Medicine, University of Nevada School of Medicine, Reno, NV 89557; or call (702) 784-6171. This position will remain open until filled. AA/EOE.

HEALTHTRUST, INC. owns 19 state-of-the-art facilities in many lovely suburban and rural communities throughout the western medical association region which have a variety of solo, group, and associate private practice opportunities for the following BE/BC physicians: Physiatrist, Family Practitioner, Internist, Pulmonologist, Cardiologist, Cardiosurgeon, Neurosurgeon, Neurologist, Psychiatrist, OB/GYN, Pediatrician, Pathologist, General Surgeon, Oncologist, Orthopedic Surgeon, Radiologist, Otolaryngologist, Urologist, Emergency Physician, Neonatologist, Gastroenterologist. Let us help you explore a practice opportunity in a community that's just right for you. No cost or obligation associated with any inquiry. For more information, send your CV to Kay Cox or Terry Moran, HealthTrust, Inc., 4525 Harding Road, Nashville, TN 37205, or call 1-800-NASH-HTI/(615) 383-4444 (collect).

PHYSICIANS WANTED

TUOLUMNE. Sierra Foothills, Yosemite area—base station hospital with 12,000 visits per year. Openings for experienced Emergency Room MDs. Outstanding mountain, recreation area in the heart of California gold country. Fee-for-service approximately $40 per hour or greater. Please send CV to Art B. Wong, MD, FACEP, Emergency Physicians' Medical Group, 1 Maritime Plaza, Ste 710, San Francisco, CA 94111.

CARDIOLOGIST, BC/BE. Invasive Cardiologist with PTCA skills to join two FACC Cardiologists in expanding ten physician Internal Medicine group in San Diego. Position available July 1988 or sooner. Reply with CV, statement of interest, and three letters of reference, to F. C. Millward, Administrator, 5111 Garfield St, La Mesa, CA 92041.

INTERNIST. To join two Primary Care Internists in private practice in beautiful far-northern California one hour below major center. Midway between Portland and San Francisco, we have a rural setting with sophisticated practice and excellent hospital facilities. Subspecialty interest desirable within primary care framework. Salary and benefits with partnership an early goal. CV and your interests to R. H. Alley, Jr, MD, 105 Oberlin Rd, Yreka, CA 96097.

CALIFORNIA. BE/BC Internist to join staff of eight Internists in 15 physician multispecialty group located in central San Joaquin Valley. Competitive starting salary and full benefits. Excellent living and practice environment. Send CV to David A. Hellstern, Administrator, Kaweah Medical Group, Inc., 222 W. Willow, Visalia, CA 93291.

OB/GYN. Tulare County is looking for a BC/BE OB/GYN to practice in an outpatient clinic, which includes inpatient duties, with 14 physicians. The county provides a benefit package which includes malpractice insurance coverage. Consider a semirural life-style with cultural amenities of metropolitan areas easily accessed and the Sierra Nevada Mountains nearby. Salary: $98,112-$103,116 annually. Send CV to: Tulare County Personnel, 2900 W. Burrel, Visalia, CA 93291; (209) 733-6266. Equal Opportunity Employer.

BC/BE CARDIOLOGIST. To join three invasive/noninvasive Cardiologists in practice, Portland, Oregon metropolitan area. Send CV to Number 76, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

SAN FRANCISCO. One hour west, growing multispecialty group needs Family Practitioner, Internist, Urgent Care, Urologist, Pediatrician, Orthopedist, ENT, Psychiatrist, Cardiologist. Good salary, benefits, incentive, early partnership. Write: Annette Pombo, Eaton Medical Group, 445 W. Eaton, Tracy, CA 95376; (209) 835-0264.

OCCUPATIONAL MEDICINE PHYSICIAN. The Virginia Mason Clinic is seeking a physician to join an expanding occupational medicine clinic system within a major medical center. The position requires experience with minor trauma and injury care. Standard clinic hours, but flexibility a must. Applicant must have a Washington State license or be license eligible; BC/BE in Occupational Medicine or Emergency Medicine preferred. The Virginia Mason Medical Center is a tertiary health care system serving the pacific northwest region. The Medical Center consists of a 220 physician multispecialty group practice, a 300-bed hospital, twelve satellite clinics, and a research center. Send CV and letter describing background and interest to Linda Hunter, Virginia Mason Clinic, 1100 Ninth Ave, PO Box 900, Seattle, WA 98111.

FAMILY PRACTITIONER. Redwood country on Pacific Ocean. University town. Prefer female and cesarean section competent. Full- or part-time. Family Practice nonprofit clinic with accent on women's and children's health care. Staffed by two OB competent Family Practitioners, one General Practitioner (practicing only women's health), two Pediatricians, and four PAs. Contact: Donald Verwayen, Administrator, Northcountry Clinic, 785 18th St, Arcata, CA 95521; (707) 822-2481.

PHYSICIANS WANTED

ONCOLOGIST/INTERNIST. BC/BE to join 21 physician primary care and multispecialty group practice in beautiful Pacific Northwest setting. Reply to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

GASTROENTEROLOGIST. 55 physician multispecialty medical group seeks full-time BC/BE Gastroenterologist. Attractive compensation and benefits. Starting date negotiable. Send CV to Don Robertson, Administrator, The Moore-White Medical Group, 266 S. Harvard Blvd, Los Angeles, CA 90004.

CALIFORNIA. BC/BE Pediatrician to join staff of three Pediatricians in 15 physician multispecialty group located in central San Joaquin Valley. Competitive starting salary and full benefits. Excellent living and practice environment. Send CV to David A. Hellstern, Administrator, Kaweah Medical Group, Inc., 222 W. Willow St, Visalia, CA 93291.

ESTABLISHED BC FAMILY PRACTITIONER in south central Washington seeks BE/BC associate with OB interest. Practice in rural, family-oriented community serving area of 45,000. Income guarantee and assistance with relocation. Ski at White Pass. Fishing and other water sports on nearby Rimrock Lake and Columbia River. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-2070, ext 202.

BE/BC FAMILY PRACTICE physician wanted to join young successful BC Family Practitioner to start new group in northeastern Colorado community. Includes OB. Service area of 25,000. Generous first year income guarantee and assistance with relocation. Only one and one-half hours from Denver. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-2070, ext 202.

PACIFIC NORTHWEST, NEAR EUGENE, OREGON. BE/BC Internist wanted to join Family Practitioner group. Share call with Internists. Minimum salary guarantee. Good schools/outdoor recreation; University of Oregon/cultural events within 30 minutes. Contact John Hoopes, Cottage Grove Hospital, 1340 Birch St, Cottage Grove, OR 97424; (503) 942-0511.

IDAHO. Family Practitioner with interest in OB wanted to join three Family Practitioners serving scenic northern Idaho community. Hospital provides complete assistance—office, salary, full benefits. BE/BC and cesarean section experience required. Enjoy outdoor recreation, rural life-style. Contact Jean Erickson, PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220-4199; (503) 256-2070.

SAN FRANCISCO BAY AREA multispecialty group seeks Internist, BC/BE, to join 26 congenial men and women delivering quality care in a combined fee-for-service, HMO/PPO setting. Bay Valley Medical Group, Attn: Don Lass, 27212 Calaroga Ave, Hayward, CA 94545; (415) 785-5000.

FAMILY PRACTICE/GENERAL PRACTICE wanted for full-time practice to work three days a week and share with another practitioner. Rural setting, good pay, nice people. Can commute for two nights a week, one hour—Sacramento, one hour and 15 minutes—Nevada City, two hours—San Francisco. Contact Charles Rath, MD, 199 E Webster St, Colusa, CA 95932; (916) 458-7739.

CALIFORNIA—NORTH SAN FRANCISCO BAY AREA. Excellent opportunity for BC/BE Family Practitioner to join growing department. Flexible starting date. Multispecialty clinic emphasizing personalized care. Full hospital privileges including ICU/CCU. No obstetrics. Very favorable call schedule. Prepaid HMO practice provides excellent salary, benefits. Forward CV to Steven Freedman, MD, Kaiser Permanente, 1550 Gateway Blvd, Fairfield, CA 94533; (707) 427-4260.

(Continued on Page 770)

(Continued from Page 768)

PHYSICIANS WANTED

EMERGENCY MEDICINE UNIVERSITY POSITION

The University of California, Davis, School of Medicine, is recruiting for a full-time faculty. The position will be at the Assistant or Associate Professor level. The Division of Emergency Medicine is undergoing rapid academic development, including the creation of an approved residency training program in Emergency Medicine. The UCDMC Emergency Department provides comprehensive emergency service and is a major trauma center in northern California. The Department is an EMT-II Base Station and Training Center and, in addition, provides medical direction for the Hospital's Helicopter Program. Candidates must be BC/BE in Emergency Medicine, and be eligible for licensure in California. Candidates should have proven teaching ability and clinical research experience. A letter outlining teaching background, interests, experience, and research, in addition to a CV, and the names of five references should be sent to:

Robert W. Derlet, MD
Chair of Emergency Medicine
Search Committee, Tr. 1219
University of California, Davis,
Medical Center
2315 Stockton Blvd
Sacramento, CA 95817

This position will be open until filled; however, applications will not be accepted after June 30, 1988. The University of California is an Affirmative Action/Equal Opportunity Employer.

PHYSICIANS WANTED

THE MISSION PARK CLINIC, SOUTHERN CALIFORNIA. The Mission Park Clinic is seeking BC/BE Internist to join a 30 physician multispecialty practice in the north coastal area of San Diego County. Reply with CV, letter of reference and compensation requirements to Donna Mills, Administrator, The Mission Park Clinic, 2201 Mission Ave, Oceanside, CA 92054.

THE VA MEDICAL CENTER, PRESCOTT, ARIZONA is recruiting for a diagnostic Radiologist with ultrasound and Nuclear Medicine training for an active outpatient/inpatient medical service. It is negotiable as to full-time or part-time. The Medical Center is a 200-bed general medical and surgical facility with a staff of approximately 500 employees. It is situated on the grounds of historic Fort Whipple. Prescott is a community of 25,000 set in the Ponderosa pine foothills of the Bradshaw range of the Rocky Mountains. At an elevation of 5,400 feet, the climate is temperate with occasional overnight snows in winter. Daytime temperature average between October and March is 58 degrees. Summer highs are in the 90s. Outdoor recreation and sports abound, year 'round tennis and golf, 100 miles to big mountain skiing. Fishing, sailing, boating on beautiful Lake Mead and Lake Powell. 200 miles to the excitement and night life of Las Vegas. All this in a quiet tree-lined community with 54 churches, a full service regional medical center, three colleges, six libraries, an excellent school system, a negligible crime rate, no pollution, low taxes, and reasonable housing prices. If you are interested in joining us in this idyllic lifestyle and possess the requisite skill and an absolutely spotless professional or employment history, send CV to Chief, Radiology Service (114), VA Medical Center, Prescott, AZ 86313 or call (602) 445-4860, ext 214. We are an Equal Opportunity Employer.

PHYSICIANS WANTED

NEAR STANFORD. Six Internists, all subspecialty trained and members of clinical faculty at Stanford, interested in an Associate with subspecialty interest and training. Should be well grounded in Internal Medicine. Send CV to Dr Bigler, El Camino Internal Medical Group, 125 South Dr, Mountain View, CA 94040.

FAMILY PRACTICE PHYSICIAN for busy primary care community clinic in the south bay area. No nights, weekends or on-call. BC/BE Spanish speaking preferred. Graduating residents encouraged to apply. Send CV to Gardner Health Center, 195 E. Virginia St, San Jose, CA 95110 or call Norma Ruiz at (408) 998-2264. EOE.

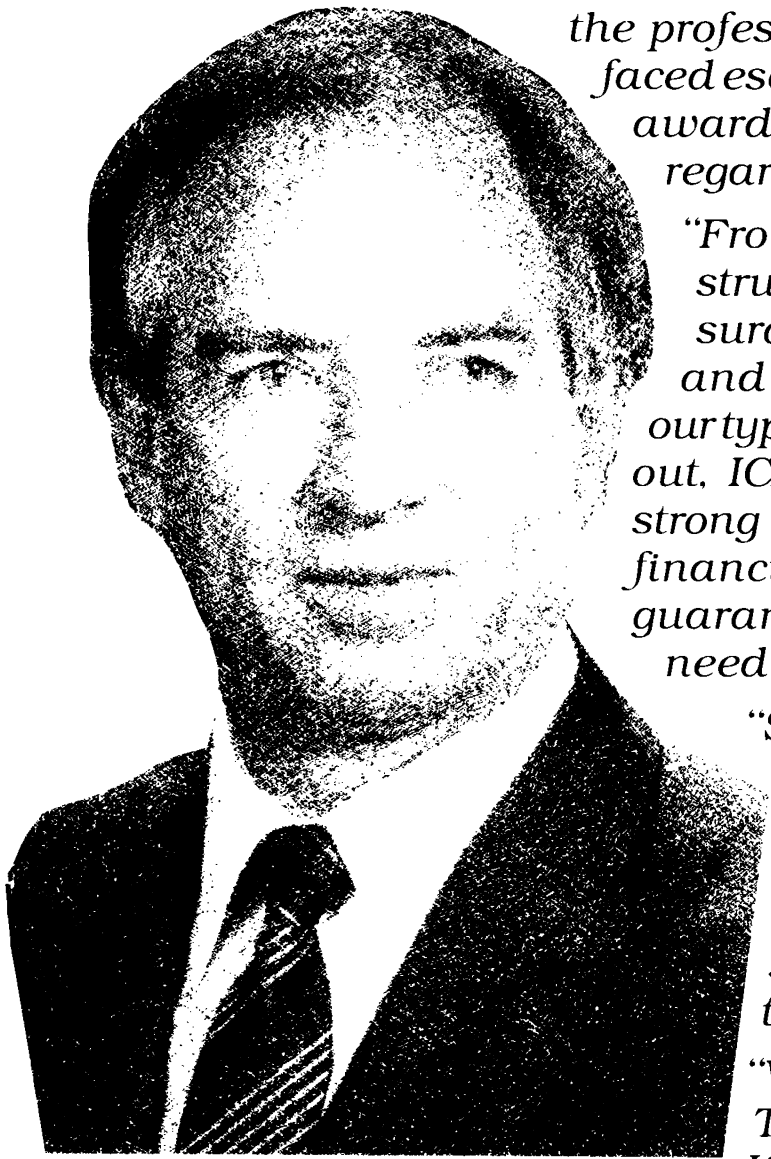
FAMILY PRACTICE. San Diego. Primary care FP/IM wanted for busy community health center. Spanish speaking preferred. Send résumé to LHFHC, 1809 National Ave, San Diego, CA 92113 or contact Bea Romo (619) 234-8171.

BC/BE NEUROLOGIST to join progressive San Francisco bay area HMO. Busy clinical practice in desirable Marin County. Competitive income and excellent benefits. EEG experience necessary/EMG expertise helpful. Position will be available July 1988. Please contact Jonathan Freudman, MD, Assistant Chief, Department of Internal Medicine, The Permanente Medical Group, 99 Montecillo Rd, San Rafael, CA 94903. AA/EOE.

THREE FAMILY PRACTITIONERS (great, great guys) in an established practice in an exciting new Encinitas office complex desire residency-trained, ambitious and compatible Family Practitioner to become part of a growing practice and office family that also includes a Psychologist and a Dietician. Salary first year, then partnership. Send CV to NCFMG, 477 N. El Camino Real, Ste A306, Encinitas, CA 92024.

(Continued on Page 774)

"We Understand Your Frustration."



DOYLE N. ROGERS, MD, FCAP, JD
Chairman, President, CEO

"You don't need to be told how tough the last few years have been in the professional liability arena. You've faced escalating premiums, escalating awards and escalating frustrations, regardless who insures you.

"From our side of the table, we've struggled with diminishing reinsurance, exhorbitant claims costs and an industry-wide change in our type of insurance policy. Throughout, ICA has strived to maintain a strong balance sheet, because our financial stability is your only real guarantee that we'll be here if you need us.

"So, we made tough and sometimes, unpopular, decisions. But the bottom line is this: We've positioned ourselves as a strong force in the professional liability business, for today and tomorrow.

"We'll be here if you need us. That's what we both want. At ICA, we're committed to protecting your practice."

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WYOMING MEDICAL SOCIETY

JANUARY 29-30, 1988 • HOLIDAY INN • CHEYENNE, WYOMING

1988 WINTER SEMINAR

MANAGING YOUR PRACTICE FOR THE CHALLENGES OF THE 1990s:
ARE YOU READY FOR A BEAR MARKET IN MEDICINE?

FRIDAY, JANUARY 29, 1988

8:45 AM Introductions
Meade O. Davis, III, MD
WMS President

MORNING SESSION BY REEVES AND COMPANY

(Participants may select *one* session in each time period—session locations will be announced)

9:00-9:50 AM **SESSION I**
Retirement Planning Under the New Tax Law

SESSION II
Taking the "Bafflegab" Out of Financial Presentations

10:00-10:45 AM **SESSION I**
All That Glitters: Investing in Gold and Precious Metals

SESSION II
Strategies for the Conservative Investor

10:45 AM Coffee Break

11:00 AM-12:00 NOON **SESSION I**
How to Invest in Stocks

SESSION II
Whatever Happened to Ginnie Mae?: U.S. Government Guaranteed Investments

12:00 NOON WMS-WMS Auxiliary Luncheon

AFTERNOON SESSION BY ROCKY MOUNTAIN PROFESSIONAL CONSULTANTS, INC.

2:00-3:00 PM *How to Prepare a Practice for Retirement*

3:00 PM Coffee Break

3:15-4:00 PM *Office Efficiency Self-Evaluation*

4:00-5:00 PM *Are You Cheating Yourself on Third Party Reimbursement?*

6:00-8:00 PM President's Reception
Sponsored by The Doctors' Company
Entertainment by the Chugwater Philharmonic String Quartet

SATURDAY, JANUARY 30, 1988

8:45 AM Welcome
Meade O. Davis, III, MD
WMS President

SATURDAY SESSION BY ROCKY MOUNTAIN PROFESSIONAL CONSULTANTS, INC.

9:00-10:10 AM *To Automate or Not to Automate—That Is the Question*

10:10 AM Coffee Break

10:30-11:30 AM *Potpourri of Personnel Principles (A Primer on Hiring and Motivating Employees)*

11:30 AM-12:15 PM *Everything You Always Wanted to Know About Practice Management But Were Afraid to Ask*
(A question and answer session on all of the morning's topics)

AUXILIARY

FRIDAY, JANUARY 29, 1988

9:00 AM Auxiliary Board Meeting

9:30 AM General Membership Meeting

12:00 NOON WMS-WMS Auxiliary Luncheon

WYOMING Medical Society

For Reservations and Information Contact:
WYOMING MEDICAL SOCIETY
P.O. Box 4009
Cheyenne, WY 82003-4009
Phone (307) 635-2424

(Continued from Page 770)

PHYSICIANS WANTED

SOUTH CENTRAL WASHINGTON COMMUNITY seeks BE/BC Internist for solo practice. Share office space with two other physicians. First year income guarantee and other assistance. Great income potential for right candidate! Progressive 38-bed hospital has CT services. Excellent schools and recreation. Contact PROSEARCH, 305 NE 102nd Ave, Portland, OR 97220; (503) 256-4488.

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GENERAL AND FAMILY PRACTICE. Will do Emergency, BE/BC, California license and DEA. 20 year's experience, call (714) 628-7643 or write R. Ervin for CV and references, 12454 Farndon Pl, Chino, CA 91710.

RADIOLOGIST. BC for locum/part-time or full-time. (209) 931-4357: evenings, weekends, some days.

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LOCUM TENENS, INC. (A Division of Jackson and Coker), can staff your practice from 2 weeks to 52 weeks, malpractice insurance for all 50 states, contact John Smith, 400 Perimeter Center Terrace, Suite 760 WJM, Atlanta, GA 30346; Tel. 1 (800) 544-1987.

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PRACTICE FOR SALE—INTERNAL MEDICINE/ SOUTHERN CALIFORNIA. Woman Internist selling established and growing practice. Male partner to remain. Scheduling flexible and ideal for person who may have concurrent obligations. Office located adjacent to hospital in Orange County. Send inquiries and/or CV to Yvonne Fox, 9701 Wilshire Blvd, Ste 850, Beverly Hills, CA 90212; (213) 934-9949.

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CALIFORNIA/NATIONWIDE. IM, Ortho, Surg, FP, Nutrition, Derm, Psych, Pulm, Neurol, OB/GYN, Oph, ENT, Urol, plus others. Bradshaw Associates, Practice Sales/Recruitment/Valuations, 21 Altamount Dr, Orinda, CA 94563; (415) 376-0762.

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INVESTOR/DEVELOPER desires to joint venture a build to suit with medical group. No dollar requirement for financially qualified group. Excellent location in Fremont, California adjacent to highly successful 11-year dental group practice treating approximately 800 patients daily. Additional space to lease for single practitioner. Dr. J. W. French, (415) 795-4160.

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I HAVE AN ARIZONA real estate license and am available to act as buyer's agent at no charge (seller pays commission). Residential, commercial, acreage. Talco Properties (602) 274-7333. Patricia Perry, MD, evenings (602) 956-3086. Investments: Brand new homes (some models) available, Phoenix area. Low down. Excellent ROI. Tenants in place. Property management available. Talco Properties (602) 274-7333. Patricia Perry, MD.

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(Continued on Page 775)

SEMINARS

MISCELLANEOUS

Rocephin® IV·IM

ceftriaxone sodium/Roche

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS AND USAGE: Rocephin is indicated for the treatment of the following infections when caused by susceptible organisms:

LOWER RESPIRATORY TRACT INFECTIONS caused by *Strep. pneumoniae, Streptococcus* species (excluding enterococci), *Staph. aureus, H. influenzae, H. parainfluenzae, Klebsiella* species (including *K. pneumoniae*), *E. coli, E. aerogenes, Proteus mirabilis* and *Serratia marcescens*.

SKIN AND SKIN STRUCTURE INFECTIONS caused by *Staph. aureus, Staph. epidermidis, Streptococcus* species (excluding enterococci), *E. cloacae, Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis* and *Pseudomonas aeruginosa*.

URINARY TRACT INFECTIONS (complicated and uncomplicated) caused by *E. coli, Proteus mirabilis, Proteus vulgaris, M. morganii* and *Klebsiella* species (including *K. pneumoniae*).

UNCOMPLICATED GONORRHEA (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including both penicillinase and nonpenicillinase producing strains.

PELVIC INFLAMMATORY DISEASE caused by *N. gonorrhoeae*.

BACTERIAL SEPTICEMIA caused by *Staph. aureus, Strep. pneumoniae, E. coli, H. influenzae* and *K. pneumoniae*.

BONE AND JOINT INFECTIONS caused by *Staph. aureus, Strep. pneumoniae, Streptococcus* species (excluding enterococci), *E. coli, P. mirabilis, K. pneumoniae* and *Enterobacter* species.

INTRA-ABDOMINAL INFECTIONS caused by *E. coli* and *K. pneumoniae*.

MENINGITIS caused by *H. influenzae, N. meningitidis* and *Strep. pneumoniae*. Ceftriaxone has also been used successfully in a limited number of cases of meningitis and shunt infections caused by *Staph. epidermidis* and *E. coli*.

SURGICAL PROPHYLAXIS: Preoperative administration of a single 1 gm dose may reduce incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (*e.g.*, vaginal or abdominal hysterectomy) and in those for whom infection at the operative site presents serious risk (*e.g.*, during coronary artery bypass surgery).

Although ceftriaxone has been shown to have been as effective as cefazolin in the prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery. When administered before indicated surgical procedures, a single 1 gm dose provides protection from most infections due to susceptible organisms for duration of procedure.

SUSCEPTIBILITY TESTING: Before instituting treatment with Rocephin, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Therapy may be instituted prior to obtaining results of susceptibility testing.

CONTRAINDICATIONS: Rocephin is contraindicated in patients with known allergy to the cephalosporin class of antibiotics.

WARNINGS: BEFORE THERAPY WITH ROCEPHIN IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind to the toxin *in vitro*.

Mild cases of colitis respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

Rarely, shadows suggesting sludge have been detected by sonograms of the gallbladder in asymptomatic and symptomatic patients. This appears to be reversible on discontinuation of therapy. In a few symptomatic patients receiving higher than usual doses, who underwent surgery, sludge containing traces of ceftriaxone was recovered from surgical specimens. Discontinue therapy in patients who develop signs or symptoms suggestive of gallbladder disease; consider conservative management.

PRECAUTIONS: *GENERAL*: Although transient elevations of BUN and serum creatinine have been observed, at the recommended dosages, the nephrotoxic potential of Rocephin is similar to that of other cephalosporins.

Ceftriaxone is excreted via both biliary and renal excretion (see Clinical Pharmacology). Therefore, patients with renal failure normally require no adjustment in dosage when usual doses of Rocephin are administered, but concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

Dosage adjustments should not be necessary in patients with hepatic dysfunction, however, in patients with both hepatic dysfunction and significant renal disease, Rocephin dosage should not exceed 2 gm daily without close monitoring of serum concentrations.

Alterations in prothrombin times have occurred rarely in patients treated with Rocephin. Patients with impaired vitamin K synthesis or low vitamin K stores (*e.g.*, chronic hepatic disease and malnutrition) may require monitoring of prothrombin time during Rocephin treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during therapy.

Prolonged use of Rocephin may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Rocephin should be prescribed with caution in individuals with a history of gastrointestinal disease, especially colitis.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Carcinogenesis: Considering the maximum duration of treatment and the class of the compound, carcinogenicity studies with ceftriaxone in animals have not been performed. The maximum

ROCEPHIN® (ceftriaxone sodium/Roche)

duration of animal toxicity studies was six months.

Mutagenesis: Genetic toxicology tests included the Ames test, a micronucleus test and a test for chromosomal aberrations in human lymphocytes cultured *in vitro* with ceftriaxone. Ceftriaxone showed no potential for mutagenic activity in these studies.

Impairment of Fertility: Ceftriaxone produced no impairment of fertility when given intravenously to rats at daily doses up to 586 mg/kg/day, approximately 20 times the recommended clinical dose of 2 gm/day.

PREGNANCY: Teratogenic Effects: Pregnancy Category B. Reproductive studies have been performed in mice and rats at doses up to 20 times the usual human dose and have no evidence of embryotoxicity, fetotoxicity or teratogenicity. In primates, no embryotoxicity or teratogenicity was demonstrated at a dose approximately three times the human dose. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: In rats, in the Segment I (fertility and general reproduction) and Segment III (perinatal and postnatal) studies with intravenously administered ceftriaxone, no adverse effects were noted on various reproductive parameters during gestation and lactation, including postnatal growth, functional behavior and reproductive ability of the offspring, at doses of 586 mg/kg/day or less.

NURSING MOTHERS: Low concentrations of ceftriaxone are excreted in human milk. Caution should be exercised when Rocephin is administered to a nursing woman.

PEDIATRIC USE: Safety and effectiveness of Rocephin in neonates, infants and children have been established for the dosages described in the Dosage and Administration section. *In vitro* studies have shown ceftriaxone, like some other cephalosporins, can displace bilirubin from serum albumin. Exercise caution before administration to hyperbilirubinemic neonates, especially prematures.

ADVERSE REACTIONS: Rocephin is generally well tolerated. In clinical trials, the following adverse reactions, which were considered to be related to Rocephin therapy or of uncertain etiology, were observed:

LOCAL REACTIONS—pain, induration or tenderness at the site of injection (1%). Less frequently reported (less than 1%) was phlebitis after I.V. administration.

HYPERSENSITIVITY—rash (1.7%). Less frequently reported (less than 1%) were pruritus, fever or chills.

HEMATOLOGIC—eosinophilia (6%), thrombocytosis (5.1%) and leukopenia (2.1%). Less frequently reported (less than 1%) were anemia, neutropenia, lymphopenia, thrombocytopenia and prolongation of the prothrombin time.

GASTROINTESTINAL—diarrhea (2.7%). Less frequently reported (less than 1%) were nausea or vomiting, and dysgeusia.

HEPATIC—elevations of SGOT (3.1%) or SGPT (3.3%). Less frequently reported (less than 1%) were elevations of alkaline phosphatase and bilirubin.

RENAL—elevations of the BUN (1.2%). Less frequently reported (less than 1%) were elevations of creatinine and the presence of casts in the urine.

CENTRAL NERVOUS SYSTEM—headache or dizziness were reported occasionally (less than 1%).

GENITOURINARY—moniliasis or vaginitis were reported occasionally (less than 1%).

MISCELLANEOUS—diaphoresis and flushing were reported occasionally (less than 1%).

Other rarely observed adverse reactions (less than 0.1%) include leukocytosis, lymphocytosis, monocytosis, basophilia, a decrease in the prothrombin time, jaundice, gallbladder sludge, glycosuria, hematuria, anaphylaxis, bronchospasm, serum sickness, abdominal pain, colitis, flatulence, dyspepsia, palpitations and epistaxis.

DOSAGE AND ADMINISTRATION: Rocephin may be administered intravenously or intramuscularly. The usual adult daily dose is 1 to 2 gm given once a day (or in equally divided doses twice a day) depending on the type and severity of the infection. The total daily dose should not exceed 4 grams.

For the treatment of serious miscellaneous infections in children, other than meningitis, the recommended total daily dose is 50 to 75 mg/kg (not to exceed 2 grams), given in divided doses every 12 hours.

Generally, Rocephin therapy should be continued for at least two days after the signs and symptoms of infection have disappeared. The usual duration is 4 to 14 days; in complicated infections longer therapy may be required.

In the treatment of meningitis, a daily dose of 100 mg/kg (not to exceed 4 grams), given in divided doses every 12 hours, should be administered with or without a loading dose of 75 mg/kg.

For the treatment of uncomplicated gonococcal infections, a single intramuscular dose of 250 mg is recommended.

For preoperative use (surgical prophylaxis), a single dose of 1 gm administered 1/2 to 2 hours before surgery is recommended.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least ten days.

No dosage adjustment is necessary for patients with impairment of renal or hepatic function, however, blood levels should be monitored in patients with severe renal impairment (*e.g.*, dialysis patients) and in patients with both renal and hepatic dysfunctions.

HOW SUPPLIED: Rocephin (ceftriaxone sodium/Roche) is supplied as a sterile crystalline powder in glass vials and piggyback bottles. The following packages are available:

Vials containing 250 mg, 500 mg, 1 gm or 2 gm equivalent of ceftriaxone; piggyback bottles containing 1 gm or 2 gm equivalent of ceftriaxone; bulk pharmacy containers containing 10 gm equivalent of ceftriaxone (NOT FOR DIRECT ADMINISTRATION).

Also supplied as a sterile crystalline powder as follows:

ADD-Vantage Vials** containing 1 gm or 2 gm equivalent of ceftriaxone.

Also supplied premixed as a frozen iso-osmotic, sterile, nonpyrogenic solution of ceftriaxone sodium in 50 mL single dose plastic containers,† as follows:

1 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.9 gm dextrose hydrous, USP added.

2 gm equivalent of ceftriaxone, iso-osmotic with approximately 1.2 gm dextrose hydrous, USP added.

NOTE: Rocephin in the frozen state should not be stored above -20°C.

*Registered trademark of Abbott Laboratories, Inc.

†Manufactured for Roche Laboratories, Division of Hoffmann-La Roche Inc., by Travenol Laboratories, Inc., Deerfield, Illinois 60015.

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* ROCEPHIN is indicated in the following infections: bacterial septicemia, bone and joint, intra-abdominal, lower respiratory tract, skin and skin structure, urinary tract, bacterial meningitis and gonorrhea. Please see summary of product information on adjacent page for indicated susceptible organisms.

Please see adjacent page for summary of product information.